a 30 gauge needle inserted posterior to the ciliary body. A dose response study using 500 ng, 100 ng, 50 ng and 10 ng of CsA and 500 ng, 100 ng and 50 ng of CsG in 25 to 50 μL of olive oil was performed. Animals were killed on day 14 (or day 28) and the eyes were fixed in 10% buffered formalin, sectioned, stained and examined for EAU.

Results

1. By using a standardized histologic grading system (Nussenblatt et al, "Local Cyclosporine Therapy for Experimental Autoimmune Uveitis in Rats," *Arch. Ophthamol.*, Vol. 103, Oct. 1985, pp. 1559–1562), a masked observer found that at equivalent dosages, CsG was 80% as effective as CsA.

2. Animals treated with CsA or CsG for 14 days manifested a "rebound" and expressed severe ocular disease.

3. The minority of animals treated for 28 days did not show evidence of EAU after 60 days.

Intravitreal CsA or CsG administrated once on day 11 after immunization with S-antigen prevented the development of EAU in the treated eye only at doses of 500 ng (see Table 2 below). The untreated control eyes did develop EAU. Assuming that the volume of a rat eye is 500 μL and that the lens has a volume of 100 μL, the peak intraocular concentration of drug was approximately 1.25 μg/ml.

TABLE 2

The Local Effect of Intravitreal CsA and CsG on EAU

Amount of Drug	Treated Eyes # Normal/Total	Untreated # Normal/Total
500 ng CsA	3/4	0/4
100 ng CsA	0/4	0/4
50 ng CsA	0/3	0/3
10 ng CsA	0/6	0/3
500 ng CsG	4/7	1/7
100 ng CsG	0/6	0/6
50 ng CsG	0/6	0/6

As is evident from the above test results regarding the local therapeutic effect of intravitreal CsA and CsG on EAU, effective prevention of EAU results if the administered dose approaches the amount of 500 ng. Thus, the scleral absorption measurements of CsA indicated in Table 1 in Example 1 above which correspond to periocular administration compare favorably with the effective therapeutic dosages of CsA and CsG indicated in Table 2.

EXAMPLE 3

Tests were also conducted to assess the topical absorption properties of CsA. Intraocular penetration of CsA in an olive oil vehicle was measured using the following methods:

Female Lewis rats, each 6 weeks of age and weighing approximately 200 g, were used for this series of experiments. Animals receiving topical and systemic medications were immunized in both hind foot pads and with a total of 50 μg of bovine S-antigen, prepared as described elsewhere (Wacker et al, "Experimental allergic uveitis: Isolation, characterization and localization of a soluble uveithopathogenic antigen from bovine retina," *J. Immunol.* 1982, 102, pp. 2360–2367), mixed with an equal portion of complete Freund's adjuvant augmented with H37 Mycobacterium tuberculosis to a concentration of 2.5 mg/mL. Animals receiving intracameral cyclosporine therapy were immunized with 30 μg of bovine S antigen prepared and mixed in the same fashion as above.

Topical Therapy. A 2% cyclosporine A solution in olive oil was the stock solution. Lower concentrations of the drug were obtained by diluting the stock solution with olive oil. Animals were treated topically with 2% and 0.2% cyclosporine A. For the determination of cyclosporine A penetration into the eye, only one drop (50 μL) of the concentrations tested was placed onto the eye.

Intracameral Administration. Using the stock 2% cyclosporine solution, 40 μL (800 μg) was injected intravitreally 11 days after S-antigen immunization. Other rats received intravitreal olive oil. This was performed using the operating room microscope for visualization and a 30 gauge needle.

Table 3 below illustrates the small amount of CsA in the vitreous after topical application.

TABLE 3

Rat Vitreous Cyclosporine Levels After Local Administration

Cyclosporine Administration	Dosage	Cyclosporine Levels in Vitreous After Application,* mg/mL 1 hr	4 hr	24 hr	48 hr	98 hr
Topical	2% solution	18	7	19	7	...
	0.2% solution	3	3	3	3	...
Intravitreal	800 ug	ND	580	390	ND	160
	80 ug	ND	60	80	ND	30

*Mean of at least four eyes per group.
ND indicates not done.

The topical application of one drop of cyclosporine at two concentrations led to levels in the intraocular contents of those eyes that were extremely low, indeed at the level approaching the sensitivity of the radioimmunoassay. Somewhat higher concentrations were noted when one drop of the 20 mg/Ml (2%) solution was used as opposed to the 2 mg/mL (0.2%) preparation.

As is evident from the results in Example 3, the intraocular penetration measurements of CsA did not provide intraocular levels of the drug as high as the absorption levels indicated for Examples 1 or 2 above. Topical administration of CsG is expected to reach similar intraocular levels because of its similar pharmacokinetic properties.

It is generally preferred that the periocular administration of CsA or CsG to the patient be used in the therapeutic treatment of ocular diseases including endogenous uveitis, corneal transplantation, vernal keratoconjunctivitis, ligneous keratoconjunctivitis, dry eye syndrome, anterior uveitis and onchocerciasis.

The invention being thus described, it will be obvious that the same may be varied in many ways. Such variations are not to be regarded as a departure from the spirit and scope of the invention, and all such modifications as would be obvious to one skilled in the art are intended to be included within the scope of the following claims.

What is claimed:

1. A method for treating ocular disease which comprises administering to a patient by periocular injection cyclosporine G in a pharmaceutically acceptable carrier in an amount effective for treating ocular disease.

2. A method for treating ocular disease which comprises administering to a patient by periocular injection cyclosporine A in a pharmaceutically acceptable carrier in an amount effective for treating ocular disease.

3. A method for treating ocular disease which comprises administering to a patient by periocular injection